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TITLE: Stabilization of tetanus toxoid in poly(DL-lactic-co-glycolic acid) microspheres for the controlled release of antigen.
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AB Sustained release of antigenically active tetanus toxoid (TT) for several weeks from biodegradable poly (DL-lactic-co-glycolic acid) (PLGA) microspheres is very important for the development of a single dose vaccine. With a view to developing such a formulation, we evaluated in the vitro release of antigenic TT from TT-containing PLGA films and microspheres stabilized with **gelatin** or **human serum albumin**. Without stabilizer, TT-containing PLGA films released low levels of antigenic TT whereas TT-containing PLGA microspheres (average size 50 microMs) released 18% of antigenic TT in 4 weeks. Inclusion of **gelatin** and **human serum albumin** increased the amount of antigenic TT released from PLGA films and microspheres. As the concentration of **gelatin** increased from 0.08% to 2.2% in PLGA films, release of antigenic TT also increased. Similar results were found with **gelatin**-stabilized TT-containing microspheres. But the significant increase by higher concentration of **gelatin** was on the initial burst during the first week. A concentration of 0.2% **gelatin** was found suitable for getting approximately 40% of antigenic TT in 4 weeks. The proportion of antigenic TT to total protein was higher during the first 2 weeks of the release studies (50% during the first week and 23% during the second week). After 2 weeks, the proportion of antigenic TT was approximately 10% for the next 2 weeks. TT-containing microspheres stabilized with **gelatin** and **human serum albumin** showed stability of antigenic TT release when these microspheres were stored at 37 degrees C for 4 weeks. **Gelatin** appears to be a good stabilizer for TT-containing microspheres, but further studies are required to increase the proportion of antigenic TT beyond 2 weeks.

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:03:11 ON 25 SEP 2002

L1 17 S VACCINE(W) (STABILISER OR STABILIZER)
L2 5 S INOSITOL AND ASCORBIC AND UREA
L3 0 S L1 AND L2
L4 5 DUP REM L2 (0 DUPLICATES REMOVED)
L5 0 S INOSITOL AND L1
L6 0 S L1 AND UREA
L7 0 S L1 AND ASCORBIC
L8 3325 S VIRUS AND UREA
L9 333 S VACCINE AND UREA
L10 74251 S ASCORBIC?
L11 1 S L9 AND L10
L12 381 S INOSITOL AND UREA
L13 0 S VACCINE AND L12
L14 1 S VACCINE AND ASCORBIC AND UREA
L15 74 S LAI AND HEPATITIS
L16 31 DUP REM L15 (43 DUPLICATES REMOVED)
L17 513014 S STABIL?
L18 1 S L16 AND L17
L19 27916 S HEPATITIS(W)A
L20 4445 S LAI
L21 0 S L19 AND L20
L22 208 S LAI AND VACCINE
L23 0 S L19 AND L22

L Number	Hits	Search Text	DB	Time stamp
2	10815	LAI	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:22
3	335	LAI and hepatitis	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:22
4	22	LAI with hepatitis	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:24
5	0	92114998.bn.	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:24
6	0	85107525.bn.	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:24
-	3260	HAV or (hepatitis adj A)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:20
-	1602	HAV or (hepatitis adj A) and human adj serum adj albumin	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/24 17:24
-	1491	HAV or (hepatitis adj A) and human adj serum adj albumin and live and vaccine and stabilizer	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/24 17:24
-	1491	HAV or (hepatitis adj A) and (human adj serum adj albumin) and live and vaccine and stabilizer	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/24 17:25
-	1491	HAV or (hepatitis adj A) and (human adj serum adj albumin) and live and vaccine and stabilizer	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/24 17:25
-	1452	HAV or (hepatitis adj A) with live with vaccine with stabilizer	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/24 17:26
-	1449	HAV or (hepatitis adj A) with live with vaccine with stabilizer with (human adj serum adj albumin)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/24 17:26

-	0	(live adj virus) with (stabilizer or stabiliser) with (protect\$3 with heat adj inactivat\$3)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 09:58
-	18	(live adj virus) with (stabilizer or stabiliser)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:29
-	39	mannitol and urea and inositol and (ascorbic adj acid) and (amino adj acid) and trehalose and gelatin	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:30
-	15	mannitol and urea and inositol and (ascorbic adj acid) and (amino adj acid) and trehalose and gelatin and virus	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:33
-	25	(stabilizer or stabiliser) and (mannitol and urea and inositol and (ascorbic adj acid) and (amino adj acid) and trehalose and gelatin)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:32
-	0	(stabilizer or stabiliser) with (mannitol and urea and inositol and (ascorbic adj acid) and (amino adj acid) and trehalose and gelatin)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:33
-	0	((live adj virus) with (stabilizer or stabiliser)) and (mannitol and urea and inositol and (ascorbic adj acid) and (amino adj acid) and trehalose and gelatin and virus)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:33
-	0	((live adj virus) and mannitol and urea and inositol and (ascorbic adj acid) and (amino adj acid) and trehalose and gelatin and virus)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:34
-	7	(live adj virus) with (stabilizer or stabiliser) and human adj serum adj albumin	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:40
-	2	(live adj virus) with (stabilizer or stabiliser) with human adj serum adj albumin	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:35
-	0	(live adj virus) with (stabilizer or stabiliser) and (ascorbic adj acid) and inositol and urea	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:42
-	0	(live adj virus) with (ascorbic adj acid) and inositol and urea	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:42
-	1	(live adj virus) and (ascorbic adj acid) and inositol and urea	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:43

	50	(live adj virus) and (ascorbic adj acid)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:43
	9	(live adj virus) and (ascorbic adj acid) and urea	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:46
	2	(live adj virus) and inositol and urea	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:44
	3	(live adj virus) and inositol and (ascorbic adj acid)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:45
	0	flavivirus adj live adj vaccine	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:46
	0	arbovirus adj live adj vaccine	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:47
	0	PIV adj live adj vaccine	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:47
	0	PIV with (live adj vaccine)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:47
	50	PIV with vaccine	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:48
	1076	PIV or RSV with vaccine	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:47
	2	PIV with vaccine.clm.	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:49
	57	measles with vaccine.clm.	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:54
	12	ascorbic with urea with inositol	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 10:55

L Number	Hits	Search Text	DB	Time stamp
1	7	(live adj virus) with (stabilizer or stabiliser) and human adj serum adj albumin	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:33
2	2014	urea with (stabilizer or stabiliser)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:33
3	0	urea with (stabilizer or stabiliser) with vaccine	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:33
4	1	urea with (stabilizer or stabiliser) with virus	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:35
5	0	urea and inositol with (stabilizer or stabiliser) with virus	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:35
6	21	urea and inositol with (stabilizer or stabiliser)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/09/25 11:35